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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/938,754	08/24/2001	Samuel J. Danishefsky	2003080-0083 (SK-943-US)	4106

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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/938,754	DANISHEFSKY ET AL.	
	Examiner	Art Unit	
	Brenda Coleman	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-22,24-28,30,33-35,38 and 57-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-21,30,33-35,38 and 57-62* is/are rejected.

7)☒ Claim(s) *22 and 24-28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 7-22, 24-28, 30, 33-35, 38 and 57-62 are pending in the application.

This action is in response to applicants' amendment filed December 12, 2003. Claims 1-3, 12-19, 21, 22, 24-26, 30 and 33 have been amended, claims 5, 6, 23, 29, 31, 32, 36, 37 and 39-56 have been canceled and claims 57-62 are newly added.

Response to Amendment

Applicant's amendments filed December 12, 2003 have been fully considered with the following effect:

1. The applicant's amendments and arguments are sufficient to overcome the improper Markush rejection of claims 1-3, 7-21, 24, 30, 33-35 and 38 labeled paragraph 3 of the last office action, which is hereby **withdrawn.**

2. The applicants' amendments to the specification deleting incorporated by reference and references to internet web pages is herein noted, however, there still remains in the specification references to internet web pages (page 86, line 15) and incorporated by reference (page 66, line 19).

3. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 30, 33-35 and 38 labeled paragraph 5 of the last office action, the applicants' arguments have been fully considered, however they were not found persuasive. Applicants argue that in light of the inhibitory effect of the inventive compounds on the Hsp90 molecular chaperone, the independent claims 30, 33 and 38 have been amended to recite treating Hsp90-dependent cancers, or inhibiting or killing Hsp90-dependent cancer cell.

Evidence involving a single compound and two types of cancer was not found sufficient to establish the enablement of claims directed to a method of treating seven types of cancer with members of a class of several compounds *In re Buting* 163 USPQ 689. The remarkable advances in chemotherapy have seen the development of specific compounds to treat specific types of cancer. The great diversity of diseases falling within the "cancer" category means that it is contrary to medical understanding that any agent (let alone a genus of thousands of compounds) could be generally effective against such diseases. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task. As stated in the MPEP, 2164.08 "[t]he Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation'." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. In re Moore, 439 F.2d 1232, 1236, 169 USPQ 236,

239 (CCPA 1971). See also Plant Genetic Sys., N.V. v. DeKalb Genetics Corp., 315 F.3d 1335, 1339, 65 USPQ2d 1452, 1455 (Fed. Cir. 2003) (alleged "pioneer status" of invention irrelevant to enablement determination)."

Claims 30, 33-35, 38 and 59-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

4. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 112 second paragraph rejections of claims 1-4, 7-22, 24-28, 30, 33-35 and 38, labeled paragraph 6 in the last office action, which are hereby **withdrawn**.

5. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 102(b) rejection of claims 1, 4, 7, 13, 18 and 21, labeled paragraph 7 in the last office action, which is hereby **withdrawn**.

6. With regards to the rejection of claims 1, 4, 13, 18, 21, 30, 33-35 and 38 under 35 U.S.C. § 102(b), labeled paragraph 8 in the last office action, the applicants' stated that the proviso spanning lines 10-17 of page 89 in originally filed claim 1 excludes such compounds as taught by Sugimura et al., U.S. Patent Nos. 5,650,430 and 5,597,846. However the proviso spanning lines 10-17 of page 89 in originally filed claim 1 does not exclude the compounds taught by Sugimura where R_B and R_D are arylalkyl, heteroaryl,

etc. See for examples the compounds 106, 107, 119, 120, 122, 123, 126, 127, 134, 135 in Table 1 to name a few.

Claims 1, 4, 13, 18, 21, 30, 33-35, 38 and 59-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Sugimura et al., U.S. Patent No. 5,650,430 and 5,597,846, for reasons of record and stated above.

7. With regards to the rejection of claims 1, 4, 7, 13, 18, 21 and 30 under 35 U.S.C. § 102(b), labeled paragraph 8 in the last office action, the applicants' stated that the proviso spanning lines 10-17 of page 89 in originally filed claim 1 excludes such compounds as taught by Lampilas et al., Tetrahedron Letters. However the proviso spanning lines 10-17 of page 89 in originally filed claim 1 does not exclude the compounds taught by Lampilas where R_1 is H. See for example the structure labeled 12.

Claims 1, 4, 7, 13, 18, 21, 30 and 59-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Lampilas et al., Tetrahedron Letters, for reasons of record and stated above.

In view of the amendment dated December 12, 2003, the following new grounds of rejections apply:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 57 and 58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The addition of claims 57 and 58 where claim 57 defines a subgenus which falls within the genus of formula I and claim 58 which is a species within the genus of formula I are not described in the specification.

Applicant is required to cancel the new matter in the reply to this Office action.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 1-4, 7-22, 24-28, 30, 33-35, 38 and 57-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a) Claims 1-4, 7-21, 30, 33-35, 38 and 59-62 are vague and indefinite in that it is not known what is meant by the proviso labeled (3) where lines 8-10 of the proviso are a duplicate of the first three lines.

b) Claim 1 recites the limitation "OR_A" in the definition of R_2. There is insufficient antecedent basis for this limitation in the claim. See lines 1 and 8 of the proviso.

c) Claim 1 recites the limitation "OR_B" in the definition of R_4. There is insufficient antecedent basis for this limitation in the claim. See lines 2 and 9 of the proviso.

d) Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by a substituted moiety in the definition of R_L in the proviso labeled (3). See lines 12-13 of the proviso.

e) Claim 4 is vague and indefinite in that it is not further limiting.

f) Claims 30, 33-35, 38 and 59-62 are vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the diseases capable of being mediated by inhibiting the growth of or killing Hsp90-dependent cancer cells. Determining whether a given disease responds or does not respond to such an inhibitor will involve undue experimentation. Suppose that a given drug, which has inhibitor properties in vitro, when administered to a patient with a certain disease, does not produce a favorable response. One cannot conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in

100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration cannot be predicted in advance. Should our drug be given as a bolus iv or in a time release po formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active in vitro, simply is not potent enough or produces such low concentrations in the blood that it is not an effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many different structurally related inhibitors must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of which are inhibitors in vitro, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the

accurate answer, and that the success of second compound arises from some other unknown property, which the second drug is capable. It is common for a drug, particularly in anti-cancer or multi-drug resistance, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation shown to affect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy, which are not themselves effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

g) Claim 57 is vague and indefinite in that it is not known what is meant by the variable R_L, which is not defined.

h) Claim 59 does not end with a period.

i) Claim 60 is a substantial duplicate of claim 59.

Claim Objections

10. Claims 22 and 24-28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 571-272-0674. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brenda Coleman

Brenda Coleman
Primary Examiner Art Unit 1624
April 30, 2004